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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/871,527	05/31/2001	Robert B. Von Dreele	S-94,792	1286

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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 10/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/871,527	VON DREELE ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) *3-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-5* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants election without traverse of Group I (claims 1-2), filed 8/16/04, is acknowledged. Claims 3-5 are withdrawn from consideration as being drawn to a non-elected Group.

Claims herein under examination are 1-2.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 1, line 11, recites the phrase "whereby a difference in the high resolution powder diffraction patterns of said first sample slurry and said second sample slurry provides a positive indication" which is vague and indefinite. It is unclear how much difference is necessary to become a positive indication. For example, if there is a minor difference caused by experimental variation or background noise, one skilled in the art would not conclude that this is a positive indication. Clarification of the metes and bounds of this phrase via clearer claim wording is requested. Claim 2 is also rejected due to its dependency from claim 1.

Claim 1, penultimate line, recites the phrase "said selected polycrystalline macromolecule material" which lacks clear antecedent basis. Two selected polycrystalline macromolecule materials are mentioned in lines 3-6. Because these materials can be interpreted to be two different types of polycrystalline macromolecule materials, it is unclear which one is being referred to in the penultimate line of the claim. Clarification of the metes and bounds of the claim via clearer claim wording is requested. Claim 2 is also rejected due to its dependency from claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. (e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nienaber et al. (P/N 6,297,021 B1) in view of Ahlem et al. (6,667,299 B1).

Nienaber et al. describe a process for screening of ligand binding to target biomolecules using X-ray crystallography via obtaining a crystal of the target biomolecule, exposing the crystal to one or more samples, and obtaining an X-ray diffraction pattern to determine whether a ligand/receptor complex was formed (abstract). Nienaber et al. describe comparing the exposed target biomolecule crystal (second sample) X-ray diffraction pattern with the X-ray diffraction pattern obtained from a non-exposed target biomolecule crystal (first sample) (claim 1) which represents diffraction patterns from the first and second samples, as stated in claim 1. Nienaber et al. describe exposing the target biomolecule by soaking it in a solution with one or more samples (abstract) which represents the sample slurry of a selected crystalline macromolecule material, one or more ligands, and a solvent, as stated in instant claim 1. Nienaber et al. describe buffers and precipitant solutions may be used to solubilize mixtures and soak them into the crystal (col. 8, lines 6-8) which represent components of the first and second sample slurries mentioned above. Nienaber et al. describe Figure 3 where X-ray diffraction dataset is collected (col. 2, lines 33-37). Nienaber et al. describe crystallographic data are collected and processed where each reflection (spot) on the diffraction pattern is assigned an index and intensity (col. 8, lines 35-38). Nienaber et al. describe converting the diffraction data to electron density maps of 3-D pictures of ligands and biomolecules (from second sample slurry) or biomolecules alone (from first sample slurry) (col. 8, lines 45-49). Nienaber et al. describe Fo-Fc maps which are subtractions of the native protein (first sample) from crystals soaked in library ligand mixture (second sample) which results in positive and negative peaks (col. 8, lines 50-56). Nienaber et al.

describe positive peaks represent ligand binding to the target biomolecule (col. 8, lines 58-61). Nienaber et al. describe comparing maps of exposed crystals with unexposed crystals to differentiate positive indications densities found in Fo-Fc maps (col. 9, lines 7-11) which represents positive indications of ligand-biomolecule complexes. Nienaber et al. describe comparing the structure of the original crystal (without ligands) with the exposed crystal structure (exposed to ligands) (col. 6, lines 50-57) which represent comparing the first and second sample slurry. Nienaber et al. describe using a method (CrystaLEAD™) as well as multiple detectors or a single synchrotron beamline which facilitates true high-throughput screening (col. 6, lines 40-49 and col. 24, lines 60-66). Nienaber et al. describe collecting high resolution data (col. 9, lines 45-46; col. 14, lines 30-32; and col. 15, lines 40-43). Nienaber et al. describe biomolecules, such as proteins (col. 1, lines 20-22), as stated in instant claim 2. Nienaber et al. do not describe polycrystalline macromolecule material or using powder diffraction data.

Ahlem et al. describe using powder X-ray diffraction (XRD) methods which have been used to characterize various crystalline compounds (col. 24, lines 17-18). Ahlem et al. state the diffraction pattern, or portions thereof, obtained from a crystalline compound is usually diagnostic for a given crystal form, although weak or very weak diffraction peaks may not always appear in replicate diffraction patterns obtained from successive batches of crystals (col. 24, lines 22-27). Peaks on XRD spectra are usually suitable to characterize or describe a crystalline material such as BrEA hemihydrate from other crystal forms that contain the same compound (col. 24, lines 31-38). Ahlem et al. describe also doing single crystal X-ray crystallography on BrEA hemihydrate (col. 25, lines 59-60).

It is noted that Paul Heiney on a webpage called "What is X-ray diffraction (XRD)" mentions that powder diffraction uses samples consisting of a collection of many small crystallites (page 4) which represents polycrystalline material. This reference is not being used as prior art, but merely to further define the powder X-ray diffraction sample used by Ahlem et al.

Nienaber et al. state that CrystaLEAD™ provides an efficient screening method for identifying compounds that will bind to a target biomolecule (col. 3, lines 9-11). Nienaber et al. state that this process has not been used before because the method was too complicated, time consuming, and problems obtaining crystals (col. 3, lines 26-38). However, Nienaber et al. state that currently available technology has overcome many of these perceived barriers (col. 3, lines 39-40). Nienaber et al. state various time saving, practical, and feasible improvements to the methodology (col. 3, lines 50-64). It would have obvious to the person of ordinary skill in the art at the time the invention was made to improve any barriers of screening ligands via crystallography, as stated by Nienaber et al. such as using various crystallographic techniques as described by Ahlem et al. Therefore, one of ordinary skill in the art would have been motivated to screen ligands (as stated by Nienaber et al.) that will bind to polycrystalline biomolecule material via powder diffraction data techniques (as stated by Ahlem et al.) as this would provide time saving procedures in high throughput screening (as stated by Nienaber et al.). One of skill in the art would have been motivated to make these modifications as single X-ray crystallography and powder crystal x-ray diffraction are two known ways of obtaining crystals, as described by Ahlem et al.

Thus, Nienaber et al. in view of Ahlem et al. motivate the limitations in claims 1 and 2.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

October 18, 2004

Ardin H. Marschel 10/22/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER